REMARKS

Favorable consideration of this application and entry of the foregoing amendments are respectfully requested.

The specification and claims have been amended to make reference to sequence identifiers and to include the Sequence Listing submitted herewith on separate sheets. Entry of the Sequence Listing does not raise the issue of new matter as the sequence information contained therein is presented in the application as originally filed. The computer readable copy of the Sequence Listing submitted herewith is the same as the attached paper copy of that Listing.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page/s is/are captioned "**Version With Markings To Show Changes Made**."

An early and favorable Action on the merits is requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at page 4, line 26:

An alternative approach has been to mutate the Fc sequence to substitute residues crucial for function. Certain target residues have been identified and published (see review by Clark 1997, *supra*). These include the N-linked carbohydrate attached to the conserved site in the C_H2 domain, certain residues in the lower hinge region (eg the sequence ELLGGP (SEQ ID NO:27)) and a proline residue at position 331 and a sequence E-x-K-x-K at positions 318-322. One recent example is disclosed by Cole et al (1997) Journal of Immunology 159, 3613-3621. In that disclosure residues 234, 235 and 237 were mutated to Alanines (or in the case of 235, sometimes to Glu). However these are all unusual residues at these positions in human IgG, thus the presence of such inappropriate amino acids may make the Fc more immunogenic or antigenic and may also lead to the loss of certain desirable Fc functions.

The paragraph beginning at page 33, line 19`:

Figure 17

This shows the Sequences of certain modified and wild-type C_H2 sequences (SEQ ID NO:4-SEQ ID NO:12), including those designated G1Δab (SEQ ID NO:1), G2Δa (SEQ ID NO:2), G1Δac (SEQ ID NO:3).

The paragraph beginning at page 34, line 29:

The oligonucleotides used to introduce the mutations were:

between the hinge and CH2 exons

MO10 5' GGA TGC AGG CTA CTC GAG GGC ACC TG 3'.(SEQ ID NO:13)

between the CH2 and CH3 exons

MO11 5' TGT CCA TGT GGC CCT GGT ACC CCA CGG GT 3'. (SEQ ID NO:14)

between the CH1 and hinge exons

MO12 5' GAG CCT GCT TCC TCT AGA CAC CCT CCC T 3' (SEQ ID NO:15)

Restriction sites are underlined.

The paragraph beginning at page 35, line 35:

The changes in CH2 at amino acid positions 327, 330 and 331 (Δa mutation) were to be introduced using the oligonucleotides:-

MO22BACK (coding strand):

5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3' (SEQ ID NO:16)

MO22 (complementary strand):

5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3' (SEQ ID NO:17)

The changes in CH2 at positions 233 to 236 (Δb and Δc mutation) were to be introduced using the oligonucleotides:-

MO7BACK (coding strand and encoding Δc mutation):

5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3' (SEQ ID NO:18)

MO21 (complementary strand and encoding Δb mutation):

5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3'. (SEQ ID NO:19)

The mutations were to be introduced by overlap extension PCR which also required the oligonucleotides MO11 and MO10BACK:

5' CAG GTG CCC TCG AGT AGC CTG CAT CC 3, (SEQ ID NO:20)

*Xho*I restriction site is underlined.

The paragraph beginning at page 37, line 30:

The Fog1 variable region DNAs (Bye, J. M., Carter, C., Cui, Y., Gorick, B. D., Songsivilai, S., Winter, G., Hughes-Jones, N. C. and Marks, J. D. (1992) Germline variable region gene segment derivation of human monoclonal anti-Rh(D) antibodies. J. Clin. Invest. 90, 2481-2490) were obtained in the vector pHEN1. They were amplified by PCR, using the oligonucleotides:-

FOG1VHBACK 5' TCC ACA GGT GTC CAC TCC CAG GTG CAT CTA CAG CAG 3' (SEQ ID NO:21)

FOG1VHFOR 5' GAG GTT GTA AGG ACT CAC CTG AGG AGA CGG TGA CCG T 3' (SEQ ID NO:22)

FOG1VKBACK 5' TCC ACA GGT GTC CAC TCC GAC ATC CAG ATG ACC CAG 3' (SEQ ID NO:23)

FOG1VKFOR 5' GAG GTT GTA AGG ACT CAC GTT TGA TCT CCA GCT TGG T 3' (SEQ ID NO:24)

The 5' portion of the insert in the vector M13VHPCR1 (Orlandi, R., Gussow, D. H., Jones, P. T. and Winter, G. (1989) Proc. Natl. Acad. Sci. USA 86, 3833), comprising the promoter and DNA encoding the signal peptide was amplified using the universal M13 reverse primer and VO3:

5' GGA GTG GAC ACC TGT GGA GA 3' (SEQ ID NO:25)

DNA, 3' of the V_H in M13VHPCR1 and representing the 5' end of the V_H-C_H intron, was obtained by PCR using the universal M13 -40 primer and VO4:

5' GTG AGT CCT TAC AAC CTC TC 3' (SEQ ID NO:26)

These two segments of DNA were joined sequentially to both the Fog-1 V_H and Fog-1 V_K amplified DNA by overlap extension PCR as described above. The *Bam*HI restriction site internal to the Fog-1 V_H was deleted by the same method using oligonucleotides which removed the recognition site without changing the amino acids encoded. The complete PCR products were cloned into M13mp19 as *Hind*III - *Bam*HI fragments and their DNA sequences confirmed.

IN THE CLAIMS:

31. (Amended) An oligonucleotide selected from:

MO22BACK: 5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3' (SEQ ID NO:16)

MO22: 5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3' (SEQ ID NO:17)

MO7BACK: 5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3' (SEQ ID NO:18)

MO21: 5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3' (SEQ ID NO:19).